HUNTINGTON’S DISEASE (HD) is an incurable genetic disorder that demonstrates an autosomal dominant pattern of inheritance with full penetrance. In HD, the Huntington gene on chromosome 4 is mutated, leading to a trinucleotide repeat expansion of CAG. Typically, HD develops when there are over 40 repeats of the CAG codon in the Huntington gene, leading to formation of the abnormal Huntington protein. Severity of symptoms and earlier onset are directly correlated with increasing numbers of CAG repeats. In addition, CAG repeat expansion tends to increase with each subsequent affected generation. Onset of HD is typically in the third or fourth decade.

The disease is characterised by choreic or ‘dance-like’ movements and progressive cognitive deterioration. Patients may also present with a host of psychiatric manifestations, including depression, psychosis and obsessive-compulsive disorder. Pathological changes associated with HD include progressive brain atrophy and neuronal degeneration, chiefly in the striatum, but also in the cerebral cortex, thalamus, subthalamic nucleus and cerebellum. Treatment of Huntington’s is symptomatic, and patients in advanced stages require extensive personal support. Life expectancy after onset of symptoms is approximately 10-25 years, although there is great variability in this range and quality of care plays an important role in delaying mortality.

Nutritional issues are a serious concern for HD sufferers from the outset of disease and throughout. They include weight loss, nutrient deficiencies and dysphagia. It is important these concerns be monitored and addressed, as they can be associated with poorer outcomes and increased mortality.

Weight loss and undernourishment

Weight loss is a particularly common finding in HD patients and is associated with worse outcomes and more rapid disease progression. HD sufferers tend to have lower body mass indices (BMI) and lower triceps and subscapular skinfold tests despite reports of increased appetite. Many patients become cachectic as the disease progresses, putting them at greater risk of opportunistic infections. Undernourishment may also lead to nutrient deficiencies, which have been cited as causes of death in a number of patients. Protein malnutrition is a particularly common finding in the advanced stages of HD.

The precise mechanisms behind weight loss in HD patients, however, remain to be elucidated. There is no evidence of malabsorption in HD sufferers, and so weight loss is believed to be the result of greater energy expenditure. Accordingly, many HD patients have increased daily energy needs when compared to control subjects. Some authors have hypothesised that severe chorea may increase energy expenditure and cause weight loss in some cases of early and mid-stage HD where choreic movements are greatest.

Pratley and colleagues found that basal metabolic rate was not elevated in HD patients, but that energy expenditure from voluntary and involuntary movements was significantly higher in HD patients, indicating a possible role for chorea. These findings were confirmed by Gaba et al. Other researchers have reported no correlation or a very weak correlation between weight loss and chorea. Weight loss is also observed in patients suffering from rigidity with no choreic symptoms and in pre-symptomatic patients, casting further doubt on the likelihood that chorea is a definite cause of cachexia. Thus, the relationship between chorea and weight loss is unlikely to be causal but remains to be fully explicated.

Another explanation for weight loss in HD involves the degeneration of somatostatin- and orexin-containing neurons in the lateral hypothalamus, a region of the brain involved in appetite control. Some reports have also indicated that HD patients have low levels of leptin, a hormone which promotes satiety, accompanied by high levels of ghrelin, a hormone which stimulates appetite; however, this finding may be secondary to disrupted sleep patterns, a common affliction among patients. Although this pattern might explain reports of increased appetite, it does not address the issue of chronic weight loss. Interestingly, one study on transgenic mice demonstrated that weight loss in HD is directly correlated with increasing numbers of CAG repeats in the Huntington’s gene, indicating a role for the Huntington gene itself – and not just the observable manifestations of the illness – in weight loss.

A number of additional factors also contribute to undernourishment in HD patients. Social factors include inadequate access to nutritious food and poor dietary planning. Patients without appropriate social support are at particularly great risk for undernourishment, as they may experience increasing difficulty in feeding and caring for themselves as physical and cognitive symptoms progress. In addition, aggravation and extreme choreic movements can make feeding difficult for both patients and caregivers. Dysphagia is another important cause of inadequate intake, as discussed below.
Dysphagia

Dysphagia, or difficulty swallowing, is a common finding among late-stage Huntington’s patients and can have fatal consequences. Dysphagia is caused by loss of control of many of the voluntary aspects of swallowing. In some patients, a tendency towards impulsivity and wolfish may also contribute to the risk of choking. Furthermore, the treatment of severe HD involves the use of neuroleptics and dopamine-depleting drugs, which may be associated with exacerbations of dysphagia due to axial rigidity and parkinsonian symptoms.

Dysphagia may be associated with asphyxia, aspiration, mandibular rigidity, inability to close the glottis, coughing on foods and choking on liquids. In addition, dysphagia may be an independent risk factor for inadequate intake, causing subsequent undernourishment and weight loss if supplementation is not implemented.

One of the most serious consequences of dysphagia is aspiration of food particles, which can potentially lead to aspiration pneumonia. Pneumonia is the most common cause of death among Huntington’s patients and it is generally accepted that aspiration pneumonia is a more common cause of death in HD patients than other forms.

Indeed, an examination of 224 post-mortem HD patients conducted by Heemskerk and Roos revealed that aspiration pneumonia has already been well established in Parkinson’s disease and the elderly and so it is likely that dietary supplementation may be helpful in stabilising and nutrient deficiencies in all stages of the disease, oral supplements can also help patients to consume the additional calories that many require.

Dysphagia probably demands the most aggressive dietetic support of all nutritional complications in HD. In mild and moderate cases, the patient’s dietary needs may be addressed with modified-texture liquids and foods and the implementation of smaller portions. Caregiver assistance at meals is critical in this population to reduce the risk of choking. In patients with severe dysphagia, PEG feeding should be seriously considered. If at all possible, PEG feeding should be discussed in the middle stages of disease progression if signs of dysphagia are present in order to prepare for the potential development of more severe dysphagia. Discussion of PEG feeding while the patient’s cognition is still intact will also ensure respect for the patient’s own directives throughout the course of the illness. PEG feeding can significantly reduce the incidence of aspiration pneumonia in severely dysphagic patients and increase quality of life for patients and caregivers.

Concluding remarks

Nutritional issues are a serious concern for patients with HD, and may include weight loss, nutrient deficiencies and dysphagia. The pathophysiology of weight loss in HD remains to be expounded upon, but may involve increased energy expenditure from voluntary and involuntary movements and reduced intake in dysphagic patients. Dysphagia is a common feature of advanced Huntington’s and can put patients at increased risk of aspiration pneumonia and asphyxiation. Nutritional issues are associated with poorer health outcomes and mortality for HD patients and should thus be appropriately monitored and addressed.

Oral supplementation may be a prudent option for patients at risk of inadequate dietary intake, and PEG feeding should be considered for patients with severe dysphagia. Future advances in the area of nutritional issues in HD patients should include specific diagnostic tools for assessing the nutritional status of the Huntington’s patient, as well as further research into the pathology of weight loss in this population.

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References